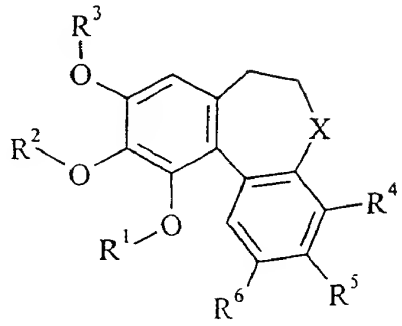
CLAIMS

1. The use of a compound of the formula I:



(I)

wherein

X is

-C(O)-, -C(S)-, -C=NOH, or -CH(R^7)- wherein R^7 is hydrogen, hydroxy, C_{1-7}alkoxy, -OR^8 or -NR^8R^9 (wherein R^8 is a group -Y^1R^{10} (wherein Y^1 is a direct bond, -C(O)-, -C(S)-, -S-, -C(O)O-, -C(O)NR^{11}-, -SO_2- or -SO_2NR^{12}- (wherein R^{11} and R^{12}, which may be the same or different, each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{10} is selected from one of the following nine groups:

1) hydrogen, C_{1-7}alkyl, C_{3-7}cycloalkyl, C_{1-4}alkylY^8C_{1-4}alkyl wherein Y^8 is as defined herein, or phenyl,

(which alkyl, cycloalkyl, alkylY^8alkyl or phenyl group may bear one or more substituents selected from:

halogeno, amino, C_{1-4}alkylamino, di(C_{1-4}alkyl)amino, hydroxy, carboxy, carbamoyl, C_{1-4}alkoxy, C_{1-4}alkylsulphanyl, C_{1-4}alkylsulphonyl, C_{1-4}alkoxycarbonylamino, C_{1-4}alkanoyl, phenyl, nitro, sulphate, phosphate,

Z^1 (wherein Z^1 represents a 5-6 membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from

oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, C_{1-4}aminoalkyl, C_{1-7}alkanoyl, cyanoC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, C_{1-4}alkylsulphonylC_{1-4}alkyl and Z^2 (wherein Z^2 is a 5-6-membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms,

selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from

oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, C_{1-4}aminoalkyl, C_{1-7}alkanoyl, cyanoC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl and C_{1-4}alkylsulphonylC_{1-4}alkyl)),

C_{1-4}alkylZ^1 (wherein Z^1 is as defined herein), and

a group $-Y^2R^{13}$ (wherein Y^2 is $-NR^{14}C(O)-$ or $-O-C(O)-$ (wherein R^{14} represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{13} is C_{1-7}alkyl, C_{3-7}cycloalkyl or a group R^{15} wherein R^{15} is a phenyl group or a 5-10-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-4 heteroatoms selected independently from O, N and S, which phenyl or aromatic heterocyclic group may bear one or more substituents selected from hydroxy, nitro, halogeno, amino, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{1-4}alkoxy, C_{1-4}hydroxyalkyl, C_{1-4}aminoalkyl, C_{1-4}alkylamino, C_{1-4}hydroxyalkoxy, carboxy, cyano, $-CONR^{16}R^{17}$ and $-NR^{18}COR^{19}$ (wherein R^{16}, R^{17}, R^{18} and R^{19}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl)));

2) R^{15} wherein R^{15} is as defined herein;

3) C_{2-7}alkenylR^{15} (wherein R^{15} is as defined herein);

4) C_{3-7}alkynylR^{15} (wherein R^{15} is as defined herein));

5) Z^1 (wherein Z^1 is as defined herein);

6) C_{1-7}alkylZ^1 (wherein Z^1 is as defined herein);

7) C_{1-7}alkylY^8Z^1 (wherein Z^1 is as defined herein and Y^8 is $-C(O)-$, $-NR^{59}C(O)-$, $-NR^{59}C(O)C_{1-4}$alkyl-, $-C(O)NR^{60}-$ or $-C(O)NR^{60}C_{1-4}$alkyl-, (wherein R^{59} and R^{60}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl, C_{1-3}hydroxyalkyl or C_{1-3}alkoxyC_{2-3}alkyl));

8) $(C_{1-7}alkyl)_cY^9Z^3$ (wherein c is 0 or 1, Z^3 is an amino acid group and Y^9 is a direct bond, $-C(O)-$ or $-NR^{61}-$ (wherein R^{61} is hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl)); and

9) C_{1-7}alkylR^{15} (wherein R^{15} is as defined herein);

and R^9 is hydrogen, C_{1-7}alkyl or C_{3-7}cycloalkyl, which alkyl or cycloalkyl group may bear one or more substituents selected from C_{1-4}alkoxy and phenyl);

R^1, R^2 and R^3 are each independently

hydrogen, PO_3H_2, sulphate, C_{3-7}cycloalkyl, C_{2-7}alkenyl, C_{2-7}alkynyl, C_{1-7}alkanoyl, a group $R^{20}C_{1-7}$alkyl (wherein R^{20} is phenyl which may bear one or more substituents selected from C_{1-4}alkyl, C_{1-4}alkoxy, C_{1-4}aminoalkyl and C_{1-4}hydroxyalkoxy), C_{1-7}alkyl or C_{1-7}alkylsulphonyl (which alkyl or alkylsulphonyl group may bear one or more substituents selected from: halogeno, amino, C_{1-4}alkylamino, di(C_{1-4}alkyl)amino, hydroxy, C_{1-4}alkoxy, C_{1-4}alkylsulphanyl, C_{1-4}alkylsulphonyl, C_{1-4}alkoxycarbonylamino, C_{1-4}alkanoyl, carboxy, phenyl, nitro, sulphate, phosphate and a group $-Y^2R^{21}$ (wherein Y^2 is $-NR^{22}C(O)-$ or $-O-C(O)-$ (wherein R^{22} represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{21} is C_{1-7}alkyl, C_{3-7}cycloalkyl or a group R^{23} wherein R^{23} is a phenyl group or a 5-10-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-4 heteroatoms selected independently from O, N and S, which phenyl or aromatic heterocyclic group may bear one or more substituents selected from hydroxy, nitro, halogeno, amino, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{1-4}alkoxy, C_{1-4}hydroxyalkyl, C_{1-4}aminoalkyl, C_{1-4}alkylamino, C_{1-4}hydroxyalkoxy, carboxy, cyano, $-CONR^{24}R^{25}$ and $-NR^{26}COR^{27}$ (wherein R^{24}, R^{25}, R^{26} and R^{27}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl)));

with the proviso that at least two of R^1, R^2 and R^3 are C_{1-7}alkyl;

R^4, R^5 and R^6 are each independently selected from:

hydrogen, $-OPO_3H_2$, phosphonate, cyano, halogeno, nitro, amino, carboxy, carbamoyl, hydroxy, C_{1-7}alkoxy, C_{1-7}alkanoyl, C_{1-7}thioalkoxy, C_{1-7}alkyl,

(which alkyl group may bear one or more substituents selected from: halogeno, amino, C_{1-4}alkylamino, di(C_{1-4}alkyl)amino, hydroxy, C_{1-4}alkoxy, C_{1-4}alkylsulphanyl, C_{1-4}alkylsulphonyl, C_{1-4}alkoxycarbonylamino, C_{1-4}alkanoyl, carboxy, phenyl, sulphate, phosphate and a group $-Y^3R^{28}$ (wherein Y^3 is $-NR^{29}C(O)-$ or $-O-C(O)-$ (wherein R^{29} represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{28} is C_{1-7}alkyl, C_{3-7}cycloalkyl or a group R^{30} wherein R^{30} is a phenyl group or a 5-10-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-4 heteroatoms selected independently from O, N and S, which phenyl or aromatic heterocyclic group may bear one or more substituents selected from hydroxy, nitro, halogeno, amino, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{1-4}alkoxy, C_{1-4}hydroxyalkyl, C_{1-4}aminoalkyl, C_{1-4}alkylamino, C_{1-4}hydroxyalkoxy, carboxy, cyano, $-CONR^{31}R^{32}$ and $-NR^{31}COR^{32}$ (wherein R^{31}, R^{32}, R^{33} and

R^{34}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl))), and

a group $-Y^4R^{35}$

(wherein Y^4 is -C(O)-, -OC(O)-, -O-, -SO-, $-SO_2-$, $-OSO_2-$, $-NR^{36}-$, $-C_{1-4}$alkyl$NR^{36}-$, $-C_{1-4}$alkylC(O)-, $-NR^{37}C(O)-$, -OC(O)O-, $-C(O)NR^{38}-$ or $-NR^{39}C(O)O-$ (wherein R^{36}, R^{37}, R^{38} and R^{39}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and

R^{35} is a sugar moiety, a mono-peptide, a di-peptide, a tri-peptide, a tetra-peptide, sulphate, hydroxy, amino, C_{1-7}alkyl, C_{1-7}alkoxy, C_{1-7}alkanoyl, C_{1-7}alkylamino, di(C_{1-7}alkyl)amino, aminoC_{1-7}alkylamino, C_{1-7}alkylaminoC_{1-7}alkylamino, C_{1-7}alkanoylaminoC_{1-7}alkyl, di(C_{1-7}alkyl)aminoC_{1-7}alkylamino, C_{1-7}alkylphosphate, C_{1-7}alkylphosphonate, C_{1-7}alkylcarbamoylC_{1-7}alkyl,

(which alkyl, alkoxy, alkanoyl, alkylamino, dialkylamino, aminoalkylamino, alkylaminoalkylamino, alkanoylaminoalkyl, dialkylaminoalkylamino, alkylphosphate, alkylphosphonate or alkylcarbamoylalkyl, may bear one or more substituents selected from:

halogeno, amino, C_{1-4}alkylamino, di(C_{1-4}alkyl)amino, hydroxy, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, C_{1-4}alkylsulphanyl, C_{1-4}alkylsulphonyl, C_{1-4}alkoxycarbonylamino, C_{1-4}alkanoyl, carboxy, phenyl, nitro, sulphate, phosphate and a group $-Y^5R^{40}$ (wherein Y^5 is $-NR^{41}C(O)-$, $-C(O)NR^{42}-$, -C(O)-O- or -O-C(O)- (wherein R^{41} and R^{42} which may be the same or different each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{40} is C_{1-7}alkyl, C_{3-7}cycloalkyl, carboxyC_{1-7}alkyl or a group R^{43} wherein R^{43} is a phenyl group, a benzyl group or a 5-10-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-4 heteroatoms selected independently from O, N and S, which phenyl, benzyl or aromatic heterocyclic group may bear one or more substituents selected from hydroxy, nitro, halogeno, amino, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{1-4}alkoxy, C_{1-4}hydroxyalkyl, C_{1-4}aminoalkyl, C_{1-4}alkylamino, C_{1-4}hydroxyalkoxy, carboxy, cyano, $-CONR^{44}R^{45}$ and $-NR^{46}COR^{47}$ (wherein R^{44}, R^{45}, R^{46} and R^{47}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl))),

R^{48} (wherein R^{48} is a phenyl group, a benzyl group or a 5-10-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-4 heteroatoms selected

independently from O, N and S, which phenyl, benzyl or aromatic heterocyclic group may bear one or more substituents selected from

hydroxy, nitro, halogeno, amino, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{1-4}alkoxy, C_{1-4}hydroxyalkyl, C_{1-4}aminoalkyl, C_{1-4}alkylamino, di(C_{1-4}alkyl)amino, di(C_{1-4}alkyl)aminoC_{1-4}alkyl, di(C_{1-4}hydroxyalkyl)aminoC_{1-4}alkyl, di(C_{1-4}aminoalkyl)aminoC_{1-4}alkyl, C_{1-4}hydroxyalkoxy, carboxy, C_{1-4}carboxyalkyl, phenyl, cyano, -CONR^{49}R^{50}, -NR^{51}COR^{52} (wherein R^{49}, R^{50}, R^{51} and R^{52}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and C_{1-4}alkylR^{53} (wherein R^{53} is as defined herein),

C_{1-7}alkylR^{48} (wherein R^{48} is as defined herein),

R^{53} (wherein R^{53} is a 5-6-membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from

oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, C_{1-4}carboxyalkyl, C_{1-4}aminoalkyl, di(C_{1-4}alkyl)aminoC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, C_{1-4}alkylsulphonylC_{1-4}alkyl and R^{54} (wherein R^{54} is a 5-6-membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from

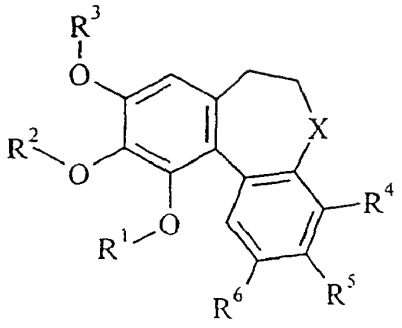
oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, C_{1-4}alkoxyC_{1-4}alkyl and C_{1-4}alkylsulphonylC_{1-4}alkyl)), or

$(CH_2)_aY^6(CH_2)_bR^{53}$ (wherein R^{53} is as defined herein, a is 0, or an integer 1-4, b is 0 or an integer 1-4 and Y^6 represents a direct bond, -O-, -C(O)-, -NR^{55}-, -NR^{56}C(O)- or -C(O)NR^{57}- (wherein R^{55}, R^{56}, and R^{57}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl), and wherein one or more of the $(CH_2)_a$ or $(CH_2)_b$ groups may bear one or more substituents selected from hydroxy, amino and halogeno));

with the proviso that R^5 is not hydroxy, alkoxy, substituted alkoxy (wherein R^5 is Y^{4}R^{35} and Y^4 is -O- and R^{35} is C_{1-7}alkyl bearing one or more substituents selected from the list given herein), $-OPO_3H_2$, -O-C_{1-7}alkanoyl or benzyloxy;

or a salt thereof, a pharmaceutically acceptable salt thereof, a solvate or hydrate thereof, or a prodrug thereof in the manufacture of a medicament for use in the production of a vascular damaging effect in warm-blooded animals such as humans.

2. A compound of the formula IIa:



(IIa)

wherein

X is

-C(O)-, -C(S)-, -C=NOH, or -CH(R^7)- wherein R^7 is hydrogen, hydroxy, C_{1-7}alkoxy, -OR^8 or -NR^8R^9 (wherein R^8 is a group -Y^1R^{10} (wherein Y^1 is a direct bond, -C(O)-, -C(S)-, -S-, -C(O)O-, -C(O)NR^{11}-, -SO_2- or -SO_2NR^{12}- (wherein R^{11} and R^{12}, which may be the same or different, each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{10} is selected from one of the following nine groups:

1) hydrogen, C_{1-7}alkyl, C_{3-7}cycloalkyl, C_{1-4}alkylY^8C_{1-4}alkyl wherein Y^8 is as defined herein, or phenyl,

(which alkyl, cycloalkyl, alkylY^8alkyl or phenyl group may bear one or more substituents selected from:

halogeno, amino, C_{1-4}alkylamino, di(C_{1-4}alkyl)amino, hydroxy, carboxy, carbamoyl, C_{1-4}alkoxy, C_{1-4}alkylsulphanyl, C_{1-4}alkylsulphonyl, C_{1-4}alkoxycarbonylamino, C_{1-4}alkanoyl, phenyl, nitro, sulphate, phosphate,

Z^1 (wherein Z^1 represents a 5-6 membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from

oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, C_{1-4}aminoalkyl, C_{1-7}alkanoyl, cyanoC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, C_{1-4}alkylsulphonylC_{1-4}alkyl and Z^2 (wherein Z^2 is a 5-6-membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from

oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, C_{1-4}aminoalkyl, C_{1-7}alkanoyl, cyanoC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl and C_{1-4}alkylsulphonylC_{1-4}alkyl)),

C_{1-4}alkylZ^1 (wherein Z^1 is as defined herein), and

a group $-Y^2R^{13}$ (wherein Y^2 is $-NR^{14}C(O)-$ or $-O-C(O)-$ (wherein R^{14} represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{13} is C_{1-7}alkyl, C_{3-7}cycloalkyl or a group R^{15} wherein R^{15} is a phenyl group or a 5-10-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-4 heteroatoms selected independently from O, N and S, which phenyl or aromatic heterocyclic group may bear one or more substituents selected from hydroxy, nitro, halogeno, amino, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{1-4}alkoxy, C_{1-4}hydroxyalkyl, C_{1-4}aminoalkyl, C_{1-4}alkylamino, C_{1-4}hydroxyalkoxy, carboxy, cyano, $-CONR^{16}R^{17}$ and $-NR^{18}COR^{19}$ (wherein R^{16}, R^{17}, R^{18} and R^{19}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl)));

2) R^{15} wherein R^{15} is as defined herein;

3) C_{2-7}alkenylR^{15} (wherein R^{15} is as defined herein);

4) C_{3-7}alkynylR^{15} (wherein R^{15} is as defined herein));

5) Z^1 (wherein Z^1 is as defined herein);

6) C_{1-7}alkylZ^1 (wherein Z^1 is as defined herein);

7) C_{1-7}alkylY^8Z^1 (wherein Z^1 is as defined herein and Y^8 is $-C(O)-$, $-NR^{59}C(O)-$, $-NR^{59}C(O)C_{1-4}$alkyl-, $-C(O)NR^{60}-$ or $-C(O)NR^{60}C_{1-4}$alkyl-, (wherein R^{59} and R^{60}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl, C_{1-3}hydroxyalkyl or C_{1-3}alkoxyC_{2-3}alkyl));

8) $(C_{1-7}alkyl)_cY^9Z^3$ (wherein c is 0 or 1, Z^3 is an amino acid group and Y^9 is a direct bond, $-C(O)-$ or $-NR^{61}-$ (wherein R^{61} is hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl)); and

9) C_{1-7}alkylR^{15} (wherein R^{15} is as defined herein);

and R^9 is hydrogen, C_{1-7}alkyl or C_{3-7}cycloalkyl, which alkyl or cycloalkyl group may bear one or more substituents selected from C_{1-4}alkoxy and phenyl);

R^1, R^2 and R^3 are each independently

hydrogen, PO_3H_2, sulphate, C_{3-7}cycloalkyl, C_{2-7}alkenyl, C_{2-7}alkynyl, C_{1-7}alkanoyl, a group $R^{20}C_{1-7}$alkyl (wherein R^{20} is phenyl which may bear one or more substituents selected from C_{1-4}alkyl, C_{1-4}alkoxy, C_{1-4}aminoalkyl and C_{1-4}hydroxyalkoxy), C_{1-7}alkyl or C_{1-7}alkylsulphonyl (which alkyl or alkylsulphonyl group may bear one or more substituents selected from:

halogeno, amino, C_{1-4}alkylamino, di(C_{1-4}alkyl)amino, hydroxy, C_{1-4}alkoxy, C_{1-4}alkylsulphanyl, C_{1-4}alkylsulphonyl, C_{1-4}alkoxycarbonylamino, C_{1-4}alkanoyl, carboxy, phenyl, nitro, sulphate, phosphate and a group $-Y^2R^{21}$ (wherein Y^2 is $-NR^{22}C(O)-$ or $-O-C(O)-$ (wherein R^{22} represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{21} is C_{1-7}alkyl, C_{3-7}cycloalkyl or a group R^{23} wherein R^{23} is a phenyl group or a 5-10-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-4 heteroatoms selected independently from O, N and S, which phenyl or aromatic heterocyclic group may bear one or more substituents selected from hydroxy, nitro, halogeno, amino, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{1-4}alkoxy, C_{1-4}hydroxyalkyl, C_{1-4}aminoalkyl, C_{1-4}alkylamino, C_{1-4}hydroxyalkoxy, carboxy, cyano, $-CONR^{24}R^{25}$ and $-NR^{26}COR^{27}$ (wherein R^{24}, R^{25}, R^{26} and R^{27}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl)));

with the proviso that at least two of R^1, R^2 and R^3 are C_{1-7}alkyl;

R^4 is

hydrogen, cyano, halogeno, nitro, amino, hydroxy, C_{1-7}alkoxy, C_{1-7}thioalkoxy, C_{1-7}alkanoyl or C_{1-7}alkyl,

(which alkyl group may bear one or more substituents selected from:
halogeno, amino, C_{1-4}alkylamino, di(C_{1-4}alkyl)amino, hydroxy, C_{1-4}alkoxy, C_{1-4}alkylsulphanyl, C_{1-4}alkylsulphonyl, C_{1-4}alkoxycarbonylamino, C_{1-4}alkanoyl, carboxy, phenyl, nitro, sulphate, phosphate and a group $-Y^3R^{28}$ (wherein Y^3 is $-NR^{29}C(O)-$ or $-O-C(O)-$ (wherein R^{29} represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{28} is C_{1-7}alkyl, C_{3-7}cycloalkyl or a group R^{30} wherein R^{30} is a phenyl group or a 5-10-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-4 heteroatoms selected independently from O, N and S, which phenyl or aromatic heterocyclic group may bear one or more substituents selected from hydroxy, nitro, halogeno, amino, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{1-4}alkoxy, C_{1-4}hydroxyalkyl, C_{1-4}aminoalkyl, C_{1-4}alkylamino, C_{1-4}hydroxyalkoxy, carboxy, cyano, $-CONR^{31}R^{32}$ and $-NR^{31}COR^{32}$ (wherein R^{31}, R^{32}, R^{33} and R^{34}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl)));

R^5 and R^6 are each independently selected from

hydrogen, $-OPO_3H_2$, phosphonate, cyano, halogeno, nitro, amino, carboxy, carbamoyl, hydroxy, C_{1-7}alkoxy, C_{1-7}alkanoyl, C_{1-7}thioalkoxy, C_{1-7}alkyl,

(which alkyl group may bear one or more substituents selected from: halogeno, amino, C_{1-4}alkylamino, di(C_{1-4}alkyl)amino, hydroxy, C_{1-4}alkoxy, C_{1-4}alkylsulphanyl, C_{1-4}alkylsulphonyl, C_{1-4}alkoxycarbonylamino, C_{1-4}alkanoyl, carboxy, phenyl, sulphate, phosphate and a group $-Y^3R^{28}$ (wherein Y^3 is $-NR^{29}C(O)-$ or $-O-C(O)-$ (wherein R^{29} represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{28} is C_{1-7}alkyl, C_{3-7}cycloalkyl or a group R^{30} wherein R^{30} is a phenyl group or a 5-10-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-4 heteroatoms selected independently from O, N and S, which phenyl or aromatic heterocyclic group may bear one or more substituents selected from hydroxy, nitro, halogeno, amino, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{1-4}alkoxy, C_{1-4}hydroxyalkyl, C_{1-4}aminoalkyl, C_{1-4}alkylamino, C_{1-4}hydroxyalkoxy, carboxy, cyano, $-CONR^{31}R^{32}$ and $-NR^{31}COR^{32}$ (wherein R^{31}, R^{32}, R^{33} and R^{34}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl))), and

a group $-Y^4R^{35}$

(wherein Y^4 is $-C(O)-$, $-OC(O)-$, $-O-$, $-SO-$, $-SO_2-$, $-OSO_2-$, $-NR^{36}-$, $-C_{1-4}$alkyl$NR^{36}-$, $-C_{1-4}$alkyl$C(O)-$, $-NR^{37}C(O)-$, $-OC(O)O-$, $-C(O)NR^{38}-$ or $-NR^{39}C(O)O-$ (wherein R^{36}, R^{37}, R^{38} and R^{39}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and

R^{35} is a sugar moiety, a mono-peptide, a di-peptide, a tri-peptide, a tetra-peptide, sulphate, hydroxy, amino, C_{1-7}alkyl, C_{1-7}alkoxy, C_{1-7}alkanoyl, C_{1-7}alkylamino, di(C_{1-7}alkyl)amino, aminoC_{1-7}alkylamino, C_{1-7}alkylaminoC_{1-7}alkylamino, C_{1-7}alkanoylaminoC_{1-7}alkyl, di(C_{1-7}alkyl)aminoC_{1-7}alkylamino, C_{1-7}alkylphosphate, C_{1-7}alkylphosphonate, C_{1-7}alkylcarbamoylC_{1-7}alkyl,

(which alkyl, alkoxy, alkanoyl, alkylamino, dialkylamino, aminoalkylamino, alkylaminoalkylamino, alkanoylaminoalkyl, dialkylaminoalkylamino, alkylphosphate, alkylphosphonate or alkylcarbamoylalkyl, may bear one or more substituents selected from:

halogeno, amino, C_{1-4}alkylamino, di(C_{1-4}alkyl)amino, hydroxy, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, C_{1-4}alkylsulphanyl, C_{1-4}alkylsulphonyl, C_{1-4}alkoxycarbonylamino, C_{1-4}alkanoyl, carboxy, phenyl, nitro, sulphate, phosphate and a group $-Y^5R^{40}$ (wherein Y^5 is $-NR^{41}C(O)-$, $-C(O)NR^{42}-$, $-C(O)-O-$ or $-O-C(O)-$ (wherein R^{41} and R^{42} which may be the same or different each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and

R^{40} is C_{1-7}alkyl, C_{3-7}cycloalkyl, carboxyC_{1-7}alkyl or a group R^{43} wherein R^{43} is a phenyl group, a benzyl group or a 5-10-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-4 heteroatoms selected independently from O, N and S, which phenyl, benzyl or aromatic heterocyclic group may bear one or more substituents selected from hydroxy, nitro, halogeno, amino, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{1-4}alkoxy, C_{1-4}hydroxyalkyl, C_{1-4}aminoalkyl, C_{1-4}alkylamino, C_{1-4}hydroxyalkoxy, carboxy, cyano, $-CONR^{44}R^{45}$ and $-NR^{46}COR^{47}$ (wherein R^{44}, R^{45}, R^{46} and R^{47}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl))),

R^{48} (wherein R^{48} is a phenyl group, a benzyl group or a 5-10-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-4 heteroatoms selected independently from O, N and S, which phenyl, benzyl or aromatic heterocyclic group may bear one or more substituents selected from

hydroxy, nitro, halogeno, amino, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{1-4}alkoxy, C_{1-4}hydroxyalkyl, C_{1-4}aminoalkyl, C_{1-4}alkylamino, di(C_{1-4}alkyl)amino, di(C_{1-4}alkyl)aminoC_{1-4}alkyl, di(C_{1-4}hydroxyalkyl)aminoC_{1-4}alkyl, di(C_{1-4}aminoalkyl)aminoC_{1-4}alkyl, C_{1-4}hydroxyalkoxy, carboxy, C_{1-4}carboxyalkyl, phenyl, cyano, $-CONR^{49}R^{50}$, $-NR^{51}COR^{52}$ (wherein R^{49}, R^{50}, R^{51} and R^{52}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and C_{1-4}alkylR^{53} (wherein R^{53} is as defined herein),

C_{1-7}alkylR^{48} (wherein R^{48} is as defined herein),

R^{53} (wherein R^{53} is a 5-6-membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from

oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, C_{1-4}carboxyalkyl, C_{1-4}aminoalkyl, di(C_{1-4}alkyl)aminoC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, C_{1-4}alkylsulphonylC_{1-4}alkyl and R^{54} (wherein R^{54} is a 5-6-membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from

oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, C_{1-4}alkoxyC_{1-4}alkyl and C_{1-4}alkylsulphonylC_{1-4}alkyl)), or

$(CH_2)_aY^6(CH_2)_bR^{53}$ (wherein R^{53} is as defined herein, a is 0, or an integer 1-4, b is 0 or an integer 1-4 and Y^6 represents a direct bond, -O-, -C(O)-, $-NR^{55}$-, $-NR^{56}C(O)$- or -

$C(O)NR^{57}$- (wherein R^{55}, R^{56}, and R^{57}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl), and wherein one or more of the $(CH_2)_a$ or $(CH_2)_b$ groups may bear one or more substituents selected from hydroxy, amino and halogeno));

with the proviso that R^5 is not hydroxy, alkoxy, substituted alkoxy (wherein R^5 is Y^4R^{35} and Y^4 is -O- and R^{35} is C_{1-7}alkyl bearing one or more substituents selected from the list given herein), $-OPO_3H_2$, -O-C_{1-7}alkanoyl or benzyloxy;

with the further proviso that at least one of R^5 or R^6 is a group $-Y^4R^{35}$ (wherein Y^4 and R^{35} are as defined herein) but with the further provisos

that when R^5 is $-Y^4R^{35}$ and R^6 is hydrogen, hydroxy, methoxy or methoxycarbonyl, $-Y^4R^{35}$ is not selected from cases wherein:

Y^4 is -C(O)-, -OC(O)-, -O-, -SO-, $-OSO_2$-, $-NR^{36}$-, $-NR^{37}C(O)$- or $-C(O)NR^{38}$- (wherein R^{36}, R^{37} and R^{38}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{35} is

a glycine, valine or lysine group, a dipeptide of glycine and valine groups, C_{1-7}alkyl, C_{1-7}alkoxy, C_{1-7}alkanoyl,

(which alkyl, alkoxy or alkanoyl may bear one or more substituents selected from: halogeno, hydroxy, and a group $-Y^5R^{40}$ (wherein Y^5 is -O-C(O)- and R^{40} is C_{1-7}alkyl)), or

R^{48} (wherein R^{48} is a tetrazolyl group (which may or may not be substituted as herein defined), a phenyl group or a benzyl group which phenyl or benzyl group may bear one or more substituents selected from C_{1-4}alkyl); and

that when R^6 is $-Y^4R^{35}$ and R^5 is hydrogen, hydroxy, methoxy or methoxycarbonyl, $-Y^4R^{35}$ is not selected from cases wherein:

Y^4 is -C(O)-, -O- or $-OSO_2$- and R^{35} is

C_{1-7}alkyl, C_{1-7}alkoxy

(which alkyl, alkoxy or alkanoyl may bear one or more substituents selected from: halogeno),

R^{48} (wherein R^{48} is a benzyl group which benzyl group may bear one or more substituents selected from C_{1-4}alkyl), or

R^{53} (wherein R^{53} is piperidinyl);

or a salt thereof.

3. The use of a compound of the formula IIa as defined in claim 2, or a salt thereof, a pharmaceutically acceptable salt thereof, a solvate or hydrate thereof, or a prodrug thereof, in the manufacture of a medicament for use in the production of a vascular damaging effect in warm-blooded animals such as humans.

4. A compound according to claim 2 wherein X is $-CH(R^7)-$ wherein R^7 is $-OR^8$ or $-NR^8R^9$ (wherein R^8 is a group $-Y^1R^{10}$ (wherein Y^1 is -C(O)-, -C(O)O- or $-C(O)NR^{11}-$ (wherein R^{11} represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{10} is as defined in claim 2) and R^9 is as defined in claim 2).

5. A compound according to claim 2 or claim 4 wherein R^1, R^2 and R^3 are each methyl.

6. A compound according to any one of claims 2, 4 or 5 wherein R^4 is hydrogen.

7. A compound according to any one of claims 2, 4, 5 or 6 wherein R^6 is hydrogen, halogeno, amino, carboxy, hydroxy, C_{1-7}alkoxy or a group Y^4R^{35} (wherein Y^4 is -C(O)-, -O- or $-OSO_2-$ and R^{35} is C_{1-7}alkyl, C_{1-7}alkoxy (which alkyl or alkoxy may bear one or more substituents selected from halogeno), R^{48} (wherein R^{48} is a benzyl group) or R^{53} (wherein R^{53} is a 5-6-membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms selected independently from O, S and N)).

8. A compound according to any one of claims 2, 4, 5, 6 or 7 wherein R^6 is hydrogen, $C(O)OCH_3$ or methoxy.

9. A compound according to any one of claims 2, 4, 5, 6, 7 or 8 wherein R^5 is hydrogen, halogeno, amino, carboxy, carbamoyl, C_{1-7}alkanoyl, C_{1-7}thioalkoxy, or a group $-Y^4R^{35}$

(wherein Y^4 is -C(O)-, -OC(O)-, -O-, -SO-, $-OSO_2-$, $-NR^{36}-$, $-NR^{37}C(O)-$ or $-C(O)NR^{38}-$ (wherein R^{36}, R^{37} and R^{38}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and

R^{35} is a sugar moiety, a mono-peptide, a di-peptide, a tri-peptide, a tetra-peptide, C_{1-7}alkyl, C_{1-7}alkoxy, C_{1-7}alkanoyl, C_{1-7}alkanoylaminoC_{1-7}alkyl,

(which alkyl, alkoxy, alkanoyl, alkanoylaminoalkyl may bear one or more substituents selected from:

halogeno, amino, hydroxy, carboxy, and a group $-Y^5R^{40}$ (wherein Y^5 is -C(O)-O- or -O-C(O)- and R^{40} is C_{1-7}alkyl or a group R^{43} wherein R^{43} is a benzyl group),

R^{48} (wherein R^{48} is a phenyl group, a benzyl group or a 5-10-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-4 heteroatoms selected independently from O, N and S, which phenyl, benzyl or aromatic heterocyclic group may bear one or more substituents selected from

hydroxy, fluoro, amino, C_{1-4}alkoxy, C_{1-4}hydroxyalkyl, C_{1-4}aminoalkyl, C_{1-4}alkylamino, di(C_{1-4}alkyl)amino, di(C_{1-4}alkyl)aminoC_{1-4}alkyl, di(C_{1-4}hydroxyalkyl)aminoC_{1-4}alkyl, di(C_{1-4}aminoalkyl)aminoC_{1-4}alkyl, C_{1-4}hydroxyalkoxy, carboxy, C_{1-4}carboxyalkyl, cyano, $-CONR^{49}R^{50}$, $-NR^{51}COR^{52}$ (wherein R^{49}, R^{50}, R^{51} and R^{52}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and C_{1-4}alkylR^{53} (wherein R^{53} is as defined herein),

C_{1-7}alkylR^{48} (wherein R^{48} is as defined herein),

R^{53} (wherein R^{53} is a 5-6-membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from

oxo, hydroxy, fluoro, chloro, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, C_{1-4}carboxyalkyl, C_{1-4}aminoalkyl, di(C_{1-4}alkyl)aminoC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, C_{1-4}alkylsulphonylC_{1-4}alkyl and R^{54} (wherein R^{54} is a 5-6-membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from

oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, C_{1-4}alkoxyC_{1-4}alkyl and C_{1-4}alkylsulphonylC_{1-4}alkyl)), or

$(CH_2)_aY^6(CH_2)_bR^{53}$ (wherein R^{53} is as defined herein, a is 0, or an integer 1-4, b is 0 or an integer 1-4 and Y^6 represents a direct bond, -O-, -C(O)-, $-NR^{55}$-, $-NR^{56}C(O)$- or $-C(O)NR^{57}$- (wherein R^{55}, R^{56}, and R^{57}, which may be the same or different, each represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl), and wherein one or more of the $(CH_2)_a$ or

Cont'd a1

$(CH_2)_b$ groups may bear one or more substituents selected from hydroxy, amino and halogeno));

with the proviso that R^5 is not alkoxy, substituted alkoxy (wherein R^5 is Y^4R^{35} and Y^4 is -O- and R^{35} is C_{1-7}alkyl bearing one or more substituents selected from the list given herein), -O-C_{1-7}alkanoyl or benzyloxy.

10. A compound according to claim 2 selected from:

(5*S*)-5-(acetylamino)-9,10,11-trimethoxy-6,7-dihydro-5*H*-dibenzo[*a*,*c*]cyclohepten-3-yl 3-{[(2*R*)-2,6-diaminohexanoyl]amino}propanoate,

(5*S*)-5-(acetylamino)-9,10,11-trimethoxy-6,7-dihydro-5*H*-dibenzo[*a*,*c*]cyclohepten-3-yl 3-[(2-aminoacetyl)amino]propanoate,

N-([(5*S*)-5-(acetylamino)-9,10,11-trimethoxy-6,7-dihydro-5*H*-dibenzo[*a*,*c*]cyclohepten-3-yl]oxymethyl)-2-morpholinoacetamide,

(2*S*,3*S*,4*S*,5*R*,6*R*)-6-{[(5*S*)-5-(acetylamino)-9,10,11-trimethoxy-6,7-dihydro-5*H*-dibenzo[*a*,*c*]cyclohepten-3-yl]oxy}-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-carboxylic acid,

N-[(5*S*)-3-(4-{4-methylpiperazin-1-ylmethyl}phenylcarbonyloxy)-9,10,11-trimethoxy-6,7-dihydro-5*H*-dibenzo[*a*,*c*]cyclohepten-5-yl]acetamide,

N-[(5*S*)-3-(4-{morpholinomethyl}phenylcarbonyloxy)-9,10,11-trimethoxy-6,7-dihydro-5*H*-dibenzo[*a*,*c*]cyclohepten-5-yl]acetamide,

(5*S*)-5-(acetylamino)-9,10,11-trimethoxy-6,7-dihydro-5*H*-dibenzo[*a*,*c*]cyclohepten-3-yl 3-[4-methylpiperazin-1-ylcarbonyl]propanoate,

5-[{(5*S*)-5-(acetylamino)-9,10,11-trimethoxy-6,7-dihydro-5*H*-dibenzo[*a*,*c*]cyclohepten-3-yl}oxycarbonyl]pentanoic acid,

4-(3-[(5*S*)-5-(acetylamino)-9,10,11-trimethoxy-6,7-dihydro-5*H*-dibenzo[*a*,*c*]cyclohepten-3-yl]oxy-3-oxopropyl)benzoic acid and

(2*S*)-*N*-[(5*S*)-5-(acetylamino)-9,10,11-trimethoxy-6,7-dihydro-5*H*-dibenzo[*a*,*c*]cyclohepten-3-yl]-2-amino-3-hydroxypropanamide,

and salts thereof.

11. A compound according to claim 2 selected from

N-[(5*S*)-3-(4-{4-methylpiperazin-1-ylmethyl}phenylcarbonyloxy)-9,10,11-trimethoxy-6,7-dihydro-5*H*-dibenzo[*a*,*c*]cyclohepten-5-yl]acetamide and

(2*S*)-*N*-[(5*S*)-5-(acetylamino)-9,10,11-trimethoxy-6,7-dihydro-5*H*-dibenzo[*a*,*c*]cyclohepten-3-yl]-2-amino-3-hydroxypropanamide,

and salts thereof.

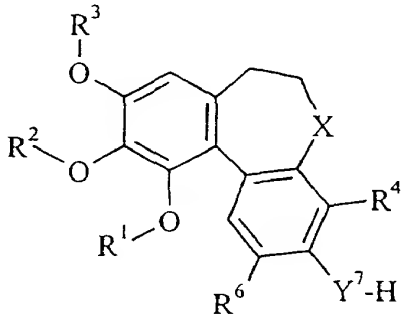
12. A compound according to claim 2 selected from

(2*S*)-*N*-[(5*S*)-5-(acetylamino)-9,10,11-trimethoxy-6,7-dihydro-5*H*-dibenzo[*a*,*c*]cyclohepten-3-yl]-2-amino-5-[(2-nitroethanimidoyl)amino]pentanamide

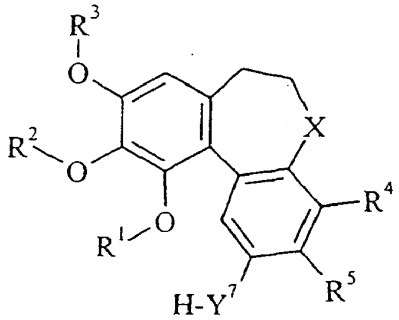
and salts thereof.

13. A process for the manufacture of a compound of formula IIa as defined in claim 2 which comprises:

(a) for the preparation of compounds of formula IIa and salts thereof in which R^5 or R^6 is a group Y^4R^{35} (wherein R^{35} is as defined in claim 2 and Y^4 is a group -OC(O)- or -NHC(O)-), the reaction of a compound of formula III or IV:



(III)



(IV)

(wherein X, R^1, R^2, R^3, R^4, R^5, R^6 are as defined in claim 2 and Y^7 is -O- or -NH-), by acylation or coupling reactions;

(b) for the preparation of compounds of formula IIa and salts thereof in which R^5 or R^6 is a group Y^4R^{35} (wherein R^{35} is C_{1-7}alkoxy which may be substituted as defined in claim 2 and Y^4 is a group -OC(O)- or -NHC(O)-), the reaction of a compound of formula III and IV, by acylation reactions;

(c) for the preparation of compounds of formula IIa and salts thereof in which R^5 or R^6 is a group Y^4R^{35} (wherein R^{35} is aminoC_{1-7}alkylamino, C_{1-7}alkylaminoC_{1-7}alkylamino, di(C_{1-7}alkyl)aminoC_{1-7}alkylamino and may be substituted as defined in claim 2, or is R^{53} (wherein

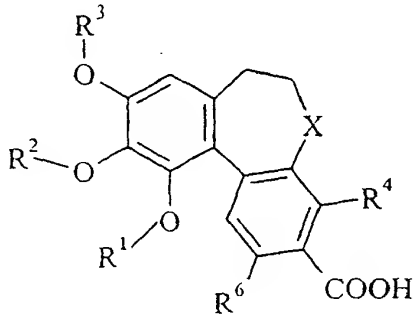
R^{53} is as defined in claim 2) and Y^4 is a group -OC(O)- or -NHC(O)-), can be prepared by the reaction of a compound of formula III or IV, acylation reactions;

(d) for the preparation of compounds of formula IIa and salts thereof in which R^5 or R^6 is a group Y^4R^{35} (wherein R^{35} is a sugar moiety and Y^4 is a group -O- or -NH-), the reaction of a compound of formula III or IV, glycosylation reactions;

(e) for the preparation of compounds of formula IIa and salts thereof in which R^5 or R^6 is a group Y^4R^{35} (wherein R^{35} is sulphate and Y^4 is a group -O- or -NH-), the reaction of a compound of formula III or IV, by sulphonylation reactions;

(f) for the preparation of compounds of formula IIa and salts thereof in which R^5 or R^6 is a group Y^4R^{35} (wherein R^{35} is C_{1-7}alkylphosphate and may be substituted as defined in claim 2 and Y^4 is a group -O- or -NH-), the reaction of a compound of formula III or IV, by phosphorylation reactions;

(g) for the preparation of compounds of formula IIa and salts thereof in which R^5 is amino the reaction of a carboxylic acid of formula V:



(V)

(wherein X, R^1, R^2, R^3, R^4 and R^6 are as defined in claim 2) via Curtius rearrangement and hydrolysis; and

(h) for the preparation of compounds of formula IIa and salts thereof in which R^5 or R^6 is chloro the reaction of a compound of formula III or IV by the Sandmeyer reaction;

and when a pharmaceutically acceptable salt of a compound of formula IIa is required, reaction of the compound obtained with an acid or base whereby to obtain the desired pharmaceutically acceptable salt.

14. A pharmaceutical composition which comprises as active ingredient a compound of formula IIa as defined in claim 2 or a pharmaceutically acceptable salt thereof in association with a pharmaceutically acceptable excipient or carrier.

15. A method for producing a vascular damaging effect in a warm-blooded animal, such as a human being, in need of such treatment which comprises administering to said animal an effective amount of a compound of formula IIa or a pharmaceutically acceptable salt thereof as defined in claim 2.